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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/056,680	01/25/2002	Teddy Kosoglou	CV01492K	9993

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SCHERING-PLOUGH CORPORATION
PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 07/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/056,680	KOSOGLOU ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-10,12-17,21-45,47 and 48* is/are pending in the application.

4a) Of the above claim(s) *4-10,12-17,21-34,38-41 and 48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,35-37,42-45 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed April 24, 2006 have been entered.

Claims 2, 11, 18-20, and 46 have been cancelled. Claims 1, 3-10, 12-17, 21-45, 47-48 are pending. Claims 4-10, 12-17, 21-34, 38-41, and 48 have been withdrawn from consideration.

Claims 1, 3, 35-37, 42-45, and 47 have been examined herein to the extent they read on the elected invention and species.

This application contains claim 48 drawn to an invention nonelected with traverse in response filed September 12, 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3, 35-37, 42-45, and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenblum et al. (EP 0720 599, reference CA from IDS received January 21, 2003), and Ullah (WO 99/47123 from IDS received January 21, 2003) in view of Frei (Proc Soc Exp Biol Med. 1999 Dec; 222(3): 196-204).

Rosenblum et al. teaches a composition comprising the compound of Formula (II), lactose, and magnesium stearate (See particularly claims 8, and 9, page 24, example 6, page 29, Examples A and B). Rosenblum et al. also teaches the active compounds therein, including the racemic mixture of compound of Formula (II), can be formulated into a tablet (See Example A and B in page 29). Rosenblum et al. also teaches the effective dosage of compound of Formula (II) as 5 to 1000mg per day (See page 17, paragraph 0065). Rosenblum et al. also teaches the active compounds therein can be combined with HMG-CoA reductase inhibitors, preferably simvastatin, for reducing cholesterol and the risk of artherosclerosis (See 5, paragraph 0028, also claims 16 and 17).

Ullah teaches a composition comprising statins, such as simvastatin, in combination with aspirin, for cholesterol lowering and treating or reducing the risk of developing atherosclerosis (See the abstract, also page 1, lines 14-18). Ullah teaches the dosage for aspirin as 50-650mg (See page 5, lines 34-37).

The primary references do not expressly teach the composition comprising the compound of formula (II) herein, aspirin, and simvastatin together. The primary

references do not expressly teach antioxidants be incorporated into the composition containing compound of formula (II) herein, aspirin, and simvastatin.

Frei teaches antioxidants, such as vitamin C and vitamin E, as useful in inhibit the atherogensis and normalize the vascular functions (See the abstract, page 198, col. 2, second paragraph, also page 199, col. 1, second paragraph, page 201, col. 2, first paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the compound of Rosenblum into the composition of Ullah. It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate antioxidant into the composition containing compound of formula (II) herein, aspirin, and simvastatin.

One of ordinary skill in the art would have been motivated to combine the compound of Rosenblum into the composition of Ullah. Combining composition of Rosenblum and that of Ullah, which are known to be useful to reduce cholesterol level and the risk of atherosclerosis individually, into a single composition useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069.

One of ordinary skill in the art would have been motivated to incorporate antioxidant into the composition containing compound of formula (II) herein, aspirin, and simvastatin. Vitamin C, an antioxidant, is known as useful to inhibit the development of atherosclerosis. Combining vitamin C with composition containing compounds of Rosenblum and Ullah, which are known to be useful to reduce cholesterol level and the

risk of atherosclerosis individually, into a single composition useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069.

Response to Arguments

Applicant's arguments filed April 24, 2006 averring the presence of unexpected benefit with the combination of ezetimibe and aspirin on platelet aggregation have been fully considered but they are not persuasive. Examiner notes that it is applicant's burden to demonstrate unexpected results over the prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In the instant case, when combining with aspirin, ezetimibe can reduce the AA induce platelet aggregation; however, the showing in Dr. Davis' declaration filed November 5, 2005 is not clear if the unexpected results are present. And even if it does, it is not commensurate with the subject matter claimed. Examiner notes that clam 1 recite a huge genus of compounds and aspirin. Furthermore, the dosage of aspirin used in the experiment is not known. The dosage of aspirin and ezetimibe resulting in unexpected benefits are not recited in the claims. Therefore, the claims are still considered properly rejected under 35 USC 103(a).

Applicant's arguments filed April 24, 2006 averring the teachings of Ullah's failure to teach aspirin to treat atherosclerosis have been considered, but are not found persuasive. In fact, the arguments have been addressed in the previous office action mailed January 24, 2006. Examiner notes that the outstanding rejection is based on the fact that the composition of Ullah, which contains aspirin, is disclosed as effective treatment for atherosclerosis. Therefore, possessing the teachings of the cited prior arts, one of ordinary skill in the art would have been motivated to combine the herein ezetimibe and the composition of Ullah into a single composition useful for the very same purpose (See *In re Kerkhoven* supra).

Applicant's remarks with regard to some of the claims do not require the presence of an optional agent such as statin have been considered, but are not found persuasive. Examiner notes that although some of the claims do not require statin, they do not exclude them neither. Therefore, possessing the teachings of the cited prior arts, one of ordinary skill in the art would have been motivated to combine the herein claimed actives into a single composition useful for the very same purpose (See *In re Kerkhoven* supra).

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

San-ming Hui

SAN-MING HUI
PRIMARY EXAMINER

Primary Examiner
Art Unit 1617